

## **REMARKS**

### **A. THE AMENDMENTS TO THE CLAIMS**

Claims 1-17, 19-56, and 65-83 are pending. Claims 17, 39-56, and 65-83 are withdrawn from consideration, and claims 1-16 and 19-38 are currently under examination insofar as the claims read on a composition or a preparation comprising an antibody that binds a peptide of NF- $\kappa$ B inducing kinase (NIK) set forth in SEQ ID NO: 7, 11, or 12.

Claim 1 has been amended to recite that the one or more antibodies are capable of detecting NF $\kappa$ B inducing kinase (NIK) in a Western blot, enzyme-linked immunosorbent assay (ELISA), or immunoprecipitation assay. Claims 1-3, 14, 19, 24-26, 30, 31, 36, 40, 41, 48, 49, 65, 66, 70, 71, 78-80, and 82 were amended to correct matters of form. Claims 8, 37, 47, and 77 were amended to remove reference to "a CDR." Claim 17 was amended to characterize the peptide as consisting essentially of the amino acid sequence set forth in SEQ ID NOs: 1-13, 15, 18-20, or 22. The amendments to the claims are fully supported by the specification at, e.g., page 17, line 23, through page 18, line 15; page 22, lines 17-25; and page 27, lines 25-24. No new matter has been added by way of the amendments.

### **B. THE OFFICE ACTION**

The Office objected to claims 1 and 2 for assertedly reciting improper Markush group language. Claims 3 and 36 were rejected under 35 U.S.C. § 112, second paragraph, for assertedly being indefinite. Claims 1-16 and 19-38 were rejected under 35 U.S.C. § 112, first paragraph, for assertedly lacking enablement. The Office rejected claims 1-16 and 30-38 under 35 U.S.C. § 102(e) for assertedly being anticipated by U.S. Patent No. 6,822,138 ("Schreiber"). Reconsideration of the rejection is respectfully requested.

### **C. THE CLAIM OBJECTIONS ARE MOOT.**

Claims 1 and 2 were subject to objection by the Office for reciting "selected from...or" or "selected from...and/or," which the Office asserted is improper phrasing for Markush groups. The objections are moot in view of the amendments to the claims.

**D. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN.**

The Office rejected claims 3 and 36 for assertedly being indefinite. In particular, claim 3 was rejected for assertedly lacking antecedent basis for “the” flanking region. Claim 3 has been amended to recite “a” flanking region, thereby rendering the rejection of claim 3 moot. With respect to claim 36, which characterized the antibody or antibody fragment of claim 30 as being murine in origin, the Office asserted that it is not clear whether the claimed antibody is human or murine. Claim 36 has been amended to recite that the polyclonal, monoclonal, chimeric, humanized or anti-anti-idiotypic antibody or antibody fragment of claim 30 is derived from mouse. One of ordinary skill in the art can recognize the metes and bounds of the claims, and the rejection under Section 112, second paragraph, should be withdrawn.

**E. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, SHOULD BE WITHDRAWN.**

Claims 1-16 and 19-38 were rejected under Section 112, first paragraph, for assertedly lacking enablement. The rejection is respectfully traversed for the reasons set forth below.

The Office raised three issues with respect to the enablement of claims 1-16 and 19-38. First, with respect to claims 8 and 37, the Office asserted that the specification does not reasonably provide enablement for an antibody fragment consisting of fewer than six complementarity determining regions (CDRs). Claims 8 and 37 have been amended to delete the reference to “a CDR,” thereby rendering the rejection moot.

Second, the Office requested Applicants’ assurance that restrictions on the availability of hybridomas Pep 7-81.1, Pep 11-355.8, and Pep 12-629-62-18 deposited with the Collection Nationale de Culture de Microorganismes (CNCM) will be removed upon the grant of a U.S. patent. In accordance with 37 C.F.R. § 1.808, the depositor’s restrictions on the availability of the deposited material will be removed upon the granting of the patent.

Finally, the Office rejected claims 1-16 and 19-38 because the specification assertedly does not enable the making or using of an antibody that binds to “any” amino acid or portion of SEQ ID NOs: 7, 11, and 12 while retaining the ability to detect NIK or a mutein, functional derivative, active fraction, circularly permuted derivative, salt, or a portion of NIK. In particular, the Office asserted that the claims encompass antibodies that bind to as few as two amino acids of SEQ ID NO: 7, 11, and 12 and variants of SEQ ID NOs: 7, 11, and 12, while only antibodies that bind to the amino acid sequences set forth in SEQ ID NOs: 7, 11, and 12 have been reduced to practice.

While Applicants disagree with the Office’s assertions, claim 1 has been amended solely in an effort to advance prosecution of the instant application to recite that the one or more antibodies or fragments thereof are capable of detecting NF- $\kappa$ B inducing kinase (NIK) in a Western blot, ELISA, or immunoprecipitation assay. The breadth of the genus of antibodies encompassed by the proposed claim is not unlimited; the antibody or fragment thereof binds to the region of the NIK protein recited in the claims and specifically detects NIK by one or more assays. The specification fully enables the anti-NIK antibodies or fragments thereof encompassed by the claims.

For example, one of ordinary skill in the art had the requisite skill to generate anti-NIK antibodies having in hand the NIK peptides encoded by the amino acid sequences recited in the claims using the specification as a guide. For example, the specification describes how to obtain antibodies by immunizing a mammal with a target antigen and isolating antibodies with desired binding specificity at, e.g., page 20, line 26, through page 21, line 2; page 22, lines 17-26; page 23, line 7, through page 24, line 8; page 24, line 20, through page 25, line 6; and page 70, line 5, through page 76, line 18. Materials and methods for generating monoclonal antibodies are described in the specification at, e.g., page 30, lines 15-24; and page 76, line 22, through page 77, line 20. Methods for recombinantly producing an antibody or antibody fragment using, for example, phage display, are provided at page 29, line 23, through page 31, line 7. The specification also teaches exemplary methods for producing antibody fragments at, e.g., page 27, line 26, through page 29, line 22. The specification further teaches methods of screening candidate antibodies for the ability to detect NIK at, e.g., page 73, line 1, through page 76, line 18. Indeed, Applicants describe exemplary monoclonal antibodies that bind SEQ ID NOs: 7, 11, and 12, and efficiently detect

NIK in Western blots, ELISA, and immunoprecipitation (page 73, line 1, through page 76, line 18).

The guidance provided by Applicants is sufficient to allow an ordinary researcher, in 2005, to generate an anti-NIK antibody or fragment thereof having the recited activity without undue experimentation. One of ordinary skill in the art could make anti-NIK antibody and antibody fragment candidates, and screen candidates for binding to NIK or a mutein, functional derivative, active fraction, circularly permuted derivative, salt, or a portion thereof using routine laboratory methods, such as those described in the specification at, e.g., page 23, line 7, through page 27, line 18. Screening even a large number of candidates does not constitute undue experimentation where, as in this instance, the disclosure provides direction and guidance on how to practice the invention. *Johns Hopkins Univ. v. Cellpro, Inc.*, 152 F.3d 1342, 1361 (Fed. Cir. 1998) (“The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention.”); *In re Wands*, 858 F.2d 731, 740 (Fed. Cir. 1988). In fact, the *In re Wands* court addressed such a factual issue and concluded that antibody-based screening did not involve a quantity of experimentation supporting a conclusion that the experimentation was undue.

The Office further asserted that one of ordinary skill would not have been able to use the antibody that binds SEQ ID NOs: 7, 11, or 12 to detect all NIK variants or a NIK fragment, mutein, functional derivative, active fraction, circularly permuted derivative, or salt. According to the Office, even slight alterations in target protein structure may abrogate antibody binding and, therefore, an antibody that binds SEQ ID NOs: 7, 11, or 12 will not bind all variants of the peptides. The alleged presence of inoperative embodiments, however, does not render a claim non-enabled when one of ordinary skill could identify operative embodiments “with expenditure of no more effort than is normally required in the art.” M.P.E.P. § 2164.08(b). Here, the ordinary practitioner need only use routine screening techniques, such as those described in the specification at, e.g., page 23, line 7, through page 27, line 18; and page 70, line 5, through page 76, line 18, to identify anti-NIK antibodies that bind a particular NIK variant. Routine screening does not constitute undue experimentation.

Additionally, the Office improperly picked one of the many uses disclosed in the application for the claimed antibody, and rejected the claims for not being enabled with respect to that particular use. The claimed antibody is not limited to a particular use in the pending claims and, therefore, any enabled use that reasonably correlates with the scope of the pending claims is sufficient to satisfy Section 112, first paragraph. See M.P.E.P. § 2164.01(c) (“If multiple uses for claimed compounds or compositions are disclosed in the application, then an enablement rejection must include an explanation, sufficiently supported by the evidence, why the specification fails to enable each disclosed use. In other words, if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention.” (Emphasis added.)).

The specification teaches multiple exemplary uses for the claimed antibody and composition including, but not limited to, regulating the biochemical activity of NIK (e.g., regulating NIK kinase activity); detecting the kinase region of NIK; and purifying or detecting a NIK fragment, mutein, functional derivative, active fraction, circularly permuted derivative, or salt (see, e.g., page 15, lines 14-18; page 16, lines 8-17; page 18, line 21, through page 19, line 21; page 34, line 3, through page 36, line 30; and page 70, line 5, through page 76, line 18). The rejection failed to explain how *each* of the disclosed uses was not enabled by the specification. That failure is unsurprising because the specification provides sufficient guidance to enable one of ordinary skill to use the claimed antibody. For instance, the specification teaches how to use the claimed anti-NIK antibody to detect both human and murine NIK. In Example 1, lysates from HeLa cells producing human NIK, mouse NIK, or fragments thereof were exposed to NIK 81 antibody, a monoclonal antibody developed against the peptide of SEQ ID NO: 7. As illustrated in Figure 9, the NIK 81 antibody detected human NIK, murine NIK, and the NIK fragments in a Western blot. The teaching of the specification is sufficient to satisfy the “use” requirement of Section 112, first paragraph.

The specification enables the full scope of claims 10-16 and 19-38, and the rejection under Section 112, first paragraph, should be withdrawn.

**F. THE REJECTION UNDER 35 U.S.C. § 102(E) SHOULD BE WITHDRAWN.**

Claims 1-16 and 30-38 were rejected under 35 U.S.C. § 102(e) for assertedly being anticipated by Schreiber. The rejection is respectfully traversed for the reasons set forth below.

Schreiber anticipates the pending claims only if the reference teaches each and every element of the pending claims. See, e.g., *Verdegaal Bros. v. Union Oil Co. of CA*, 814 F.2d 628, 631 (Fed. Cir. 1987). Claims 1-16 and 30-38 are directed to a preparation or pharmaceutical composition comprising one or more polyclonal, monoclonal, chimeric, humanized, human or anti-anti-idiotypic antibodies and/or fragments thereof capable of specifically binding an amino acid sequence set forth in SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 15, 18, 19, 20, or 22, or a portion of said amino acid sequence. The referenced amino acid sequences encode subregions or fragments of the NIK protein. Schreiber discloses a genus of antibodies that bind NIK, and does not teach each and every feature of the instant antibody or antibody fragment that selectively binds an amino acid sequence as recited in the pending claims. It is well-settled that disclosure of a genus does not anticipate a claimed species. *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1367 (Fed. Cir. 2004) (explaining that “[a] prior art reference that discloses a genus still does not inherently disclose all species within that broad category”). Indeed, the reference does not teach or suggest the specific portion of NIK to which the claimed antibody binds, nor does the reference teach a subset of antibodies that specifically binds the recited NIK fragments.

Despite the failure of Schreiber to teach each and every element of any of the pending claims, the Office asserts that applicants must prove that the described genus of polyclonal antibodies would not bind to the recited NIK fragments, suggesting that the disclosed genus of antibodies inherently meets the limitations of the pending claims. To rely on a theory of inherency, however, the Office must provide “a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art.” *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Interf. 1990). “The mere fact that a certain thing may result from a given set of circumstances is not sufficient.” *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (citations omitted). The Office failed to present evidence or reasoning showing

that any prior art antibodies would necessarily bind to the portions of NIK recited in the claims and, therefore, has not met the Office's burden. Without such evidence or reasoning, the Office cannot require an applicant to prove that the prior art does not possess the claimed characteristic. See *Ex parte Jurg Zimmerman* 2003 WL 25277881, \*4 (Bd. Pat. App. & Interf. 2003), quoting *Ex parte Skinner*, 2 U.S.P.Q.2d 1788 (Bd. Pat. App. & Interf. 1986).

Additionally, claim 1 recites that the antibodies or fragments thereof are capable of detecting NF- $\kappa$ B inducing kinase (NIK) in a Western blot, ELISA, or immunoprecipitation assay, and the specification provides evidence that not all polyclonal anti-NIK antibodies detect NIK in a Western blot or immunoprecipitation assay. See the Example in the specification, which reports results of a detection assay using commercially available polyclonal anti-NIK antibodies. As explained at page 73, lines 1-10, commercially available polyclonal antibodies raised against NIK either did not detect NIK or suffered from batch-to-batch variation. Accordingly, Applicants have shown that features of the claimed antibodies are not necessarily found in the genus of anti-NIK antibodies of Schreiber. The reference fails to explicitly or inherently disclose the particular anti-NIK antibodies of the pending claims. Therefore, the rejection of claims 1-16 and 30-38 under 35 U.S.C. § 102(e) over Schreiber is improper and should be withdrawn.

#### G. CONCLUSION

Applicants submit that the pending application is in condition for allowance. The Examiner is invited to contact the undersigned attorney by telephone if there are issues or questions concerning this submission that might be efficiently resolved in that manner.

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Respectfully submitted,

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